Claims

1. An aqueous G-CSF-containing composition comprising, as buffer substances, succinate and/or tartrate in the form of the free acid and/or of a salt thereof,

   compositions having a tartrate concentration of less than 2 mM and a pH value of ≤ 4.0, which do not contain succinate as a buffer substance, being excluded.

2. The composition according to claim 1, wherein the pH value of the composition is between 3.5 and 6.0, preferably between 4.0 and 5.8, and more preferably between 4.5 and 5.5.

3. The composition according to claim 1 or 2, wherein the salt of the succinic acid and/or of the tartaric acid is selected from alkali, alkaline earth, or ammonium salts.

4. The composition according to claim 3, wherein the salt of the succinic acid and/or the tartaric acid is the disodium salt.

5. The composition according to any one of claims 1 to 4, wherein succinate and/or tartrate are present in a concentration of from 0.5 to 150 mM, preferably of from 1 to 100 mM, and in more preferably of from 1 to 50 mM.

6. The composition according to any one of claims 1 to 5, wherein G-CSF is present in a concentration of from 0.0001 to 5 mg/ml, in particular of from 0.0005 to 4 mg/ml, and preferably of from 0.01 to 1.5 mg/ml.

7. The composition according to any one of claims 1 to 6, further comprising one or more additional stabilizers and/or adjuvants and inactive ingredients, in particular those selected from the group consisting of surfactants, isotonizing agents, amino acids, reducing agents, antioxidants, complexing agents, and chaotropic agents.

8. The composition according to claim 7, wherein the surfactant is a non-ionogenic surfactant selected from the group consisting of polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monooleate, polyoxyethylene sorbitan monostearate, polyoxyethylene-sorbitan mono palmitate, polyoxyethylene sorbitan trioleate and polyoxyethylene sorbitan tristearate.

9. The composition according to claim 7, wherein the complexing agent is citrate.

10. The composition according to claim 7, wherein the isotonizing agent is mannitol and/or sorbitol.

11. The composition according to any one of claims 1 to 10 as a pharmaceutical preparation.

12. The composition according to claim 11, wherein the pharmaceutical preparation is a solution for injection or infusion.

13. A lyophilisate or a powder comprising G-CSF as well as succinate and/or tartrate in the form of the free acid and/or of a salt thereof.

14. The lyophilisate or powder according to claim 13, wherein the salt of the succinic acid and/or of the tartaric acid is selected from alkali, alkaline earth, or ammonium salts.

15. The lyophilisate or powder according to any one of claims 13 or 14, wherein the salt of the succinic acid and/or of the tartaric acid is the disodium salt.

16. The lyophilisate or powder according to any one of claims 13 to 15, further comprising one or more additional stabilizers and/or adjuvants and inactive ingredients, in particular selected from the group consisting of surfactants, isotonizing agents, amino acids, reducing agents, antioxidants, complexing agents, and chaotropic agents.

17. The lyophilisate or powder according to claim 16, wherein the complexing agent is citrate.

18. The lyophilisate or powder according to any one of claims 13 to 17, obtainable by lyophilization or spray-drying, respectively, of an aqueous G-CSF-containing composition comprising, as buffer substances, succinate and/or tartrate in the form of the free acid and/or of a salt thereof.

19. A pharmaceutical kit, comprising physically separated:

a) a G-CSF-containing lyophilisate or powder; and

b) an aqueous solvent comprising succinate and/or tartrate in the form of the free acid and/or of a salt thereof.

20. The pharmaceutical kit according to claim 19, wherein the G-CSF-containing lyophilisate or powder comprises succinate and/or tartrate in the form of the free acid and/or of a salt thereof.

21. The pharmaceutical kit according to claim 19 or 20, wherein the lyophilisate or powder and/or the aqueous solvent further comprise one or more additional stabilizers and/or adjuvants and inactive ingredients, in particular selected from the group consisting of surfactants, isotonizing agents, amino acids, reducing agents, antioxidants, complexing agents, and chaotropic agents.

22. A method for preparing a composition according to any one of claims 1 to 12, comprising dissolving of G-CSF in an aqueous solvent comprising succinate and/or tartrate in the form of the free acid and/or of a salt thereof as buffer substances.

23. A method for preparing a lyophilisate or a powder according to any one of claims 13 to 18, comprising lyophilization or spray-drying of a composition according to any one of claims 1 to 10.

24. Use of succinate and/or tartrate, in the form of the free acid and/or of a salt thereof, for stabilizing G-CSF.

25. Use of a composition according to any one of claims 1 to 10 or of a lyophilisate or powder according to any one of claims 13 to 18 for the manufacture of pharmaceutical preparations.

26. Use according to claim 25, wherein the pharmaceutical preparations comprise hydrogels or liposomes.

Amended Claims

1. A stable aqueous G-CSF-containing composition comprising, as a buffer substance, succinate in the form of the free acid and/or of a salt thereof in a concentration of from 0.5 to 100 mM.

2. The composition according to claim 1, wherein the pH value of the composition is between 3.5 and 6.0, preferably between 4.0 and 5.8, and more preferably between 4.5 and 5.5.

3. The composition according to claim 1 or 2, wherein the salt of the succinic acid is selected from alkali, alkaline earth, or ammonium salts.

4. The composition according to claim 3, wherein the salt of the succinic acid is the disodium salt.

5. The composition according to any one of claims 1 to 4, wherein the succinate is present in a concentration of from 1 to 50 mM.

6. The composition according to any one of claims 1 to 5, wherein G-CSF is present in a concentration of from 0.0001 to 5 mg/ml, in particular of from 0.0005 to 4 mg/ml, and preferably of from 0.01 to 1.5 mg/ml.

7. The composition according to any one of claims 1 to 6, further comprising one or more further stabilizers and/or adjuvants and inactive ingredients, in particular selected from the group consisting of surfactants, isotonizing agents, amino acids, reducing agents, antioxidants, complexing agents, and chaotropic agents.

8. The composition according to claim 7, wherein the surfactant is a non-ionogenic surfactant selected from the group consisting of polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monooleate, polyoxyethylene sorbitan monostearate, polyoxyethylene-sorbitan monopalmitate, polyoxyethylene sorbitan trioleate and polyoxyethylene sorbitan tristearate.

9. The composition according to claim 7, wherein the complexing agent is citrate.

10. The composition according to claim 7, wherein the isotonizing agent is mannitol and/or sorbitol.

11. The composition according to any one of claims 1 to 10 as a pharmaceutical preparation.

12. The composition according to claim 11, wherein the pharmaceutical preparation is a solution for injection or infusion.

13. A lyophilisate or a powder comprising G-CSF as well as succinate in the form of the free acid and/or of a salt thereof, obtainable by lyophilization or spray-drying, respectively, of an aqueous G-CSF-containing composition according to any one of claims 1 to 10.

14. The lyophilisate or powder according to claim 13, wherein the salt of the succinic acid is selected from alkali, alkaline earth, or ammonium salts.

15. The lyophilisate or powder according to any one of claims 13 or 14, wherein the salt of the succinic acid is the disodium salt.

16. The lyophilisate or powder according to any one of claims 13 to 15, further comprising one or more additional stabilizers and/or adjuvants and inactive ingredients, in particular selected from the group consisting of surfactants, isotonizing agents, aminoacids, reducing agents, antioxidants, complexing agents and chaotropic agents.

17. The lyophilisate or powder according to claim 16, wherein the complexing agent is citrate.

18. A pharmaceutical kit comprising physically separated:

a) a G-CSF-containing lyophilisate or powder; and

b) an aqueous solvent comprising succinate in the form of the free acid and/or of a salt thereof.

19. The pharmaceutical kit according to claim 18, wherein the G-CSF-containing lyophilisate or powder comprises succinate in the form of the free acid and/or of a salt thereof.

20. The pharmaceutical kit according to claim 18 or 19, wherein the lyophilisate or powder and/or the aqueous solvent further comprise one or more additional stabilizers and/or adjuvants and inactive ingredients, in particular selected from the group consisting of surfactants, isotonizing agents, aminoacids, reducing agents, antioxidants, complexing agents and chaotropic agents.

21. A method for preparing aqueous compositions that are stable in storage according to any one of claims 1 to 12, comprising dissolving of G-CSF in an aqueous solvent comprising succinate in the form of the free acid and/or of a salt thereof in a concentration of from 0.5 to 100 mM as a buffer substance.

22. A method for preparing a lyophilisate or a powder according to any one of claims 13 to 17, comprising lyophilizing or spray-drying a composition according to any one of claims 1 to 10.

23. Use of succinate in the form of the free acid and/or of a salt thereof for stabilizing G-CSF in aqueous compositions and lyophilisates and powders obtainable therefrom.

24. Use of a composition according to any one of claims 1 to 10 or of a lyophilisate or powder according to any one of claims 13 to 17 for preparing pharmaceutical preparations.

25. Use according to claim 24, wherein the pharmaceutical preparations comprise hydrogels or liposomes.